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REVIEW ARTICLE

Thrombophilia screening in asymptomatic children

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Abstract

Children with a family history of thrombophilia and/or thrombosis are often referred to pediatric thrombosis centers for evaluation. This article reviews the risks and benefits of thrombophilia testing in this unique population. The article also reviews an approach to testing including a step-wise evaluation and involvement of a genetic counselor.

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Introduction

Testing for hypercoaguability is one of the most commonly ordered genetic tests in medical practices and through 'direct to consumer testing' [1]. Qualitative research has shown that parents with thrombophilia frequently ask whether or not their child(ren) should be screened for thrombophilia [2–4], and one of

Abbreviations: VTE, venous thromboembolism; ACMG, American College of Medical Genetics; FVL, factor V Leiden; PT, prothrombin G20210A; AAP, American Academy of Pediatrics; NICU, neonatal intensive care unit; CVL, central venous line; EPCOT, European Prospective Cohort on Thrombophilia; OCPs, oral contraceptives.

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the reasons for referral to a pediatric hemostasis and thrombosis center is a family history of thrombosis and/or thrombophilia. Children may be referred because a parent or sibling has thrombophilia or because a distant relative has thrombophilia. Children may also be referred because their mother was diagnosed with thrombophilia during pregnancy. One of the questions during the evaluation of the child is whether or not to test the child for thrombophilia. The Subcommittee for Perinatal and Pediatric Thrombosis of the Scientific and Standardization Committee of the International Society of Thrombosis and Haemostasis recommend a step-wise thrombophilia evaluation for children with venous thrombosis, but this statement does not address screening in asymptomatic children with a family history of thrombosis or thrombophilia [5].

When considering whether or not to screen a child without a history of thrombosis for thrombophilia the benefits and risks of screening that individual should be considered (Table 1) [6]. The objective of this review is to discuss thrombophilia screening in children with a family history of venous thromboembolism (VTE) and/or thrombophilia.

Table 1 Pros and cons of genetic testing for thrombophilia in children

Pros	Cons
• Helps family understand thrombophilia	• May not be of immediate benefit
• Provides impetus to implement lifestyle changes to reduce risk of thrombosis	• Time consuming and expensive; not proven to be cost-effective
• Provides impetus to avoid risk factors such as prolonged sitting or standing during travel	• Thrombophilia may be interpreted as a disease rather than a risk factor-advent of the 'unpatient'
• Provides impetus to avoid thrombogenic drugs	• Results may be misinterpreted by family or general practitioner
• Allows parents time to teach children about risk factor	• Testing may be incomplete or inaccurate
• Health care providers can use information to tailor primary prophylactic anticoagulation during high-risk situations	• Personal costs due to false positive results, which can lead to distress and possible unnecessary treatment
• May reduce the occurrence of VTE in the general population	• May create false sense of security
• May reduce the occurrence of VTE in a given family	• May trigger discrimination in obtaining medical or life insurance
	• Parent may feel anxious or guilty
	• Women may not be able to obtain OCPs

Screening programs

Within the medical field, there are many types of screening tests. For children without a history of VTE, we are interested in screening for predisposition to disease. Screening for thrombophilia is similar to cholesterol screening for cardiovascular disease because the results indicate whether someone has an increased risk of thrombosis rather than delineating whether or not someone will have a VTE. The goal of screening is to identify those individuals who are more likely to be helped than harmed by the results of the test. In the case of thrombophilia, the benefit of preventing VTE should be weighed against the risk of the preventive treatment and risks of labeling someone as having a disease [7].

It is useful to consider criteria that define an acceptable screening test. Many criteria for screening programs have been proposed, and most are similar to those proposed by Wilson and Jungner in a 1968 World Health Organization report [8]. Modified criteria (Table 2) were proposed by the report from the Crossroads 99 conference, held in Toronto, Canada, in October 1999, in conjunction with an international symposium examining the ethical, legal, and socio-behavioral implications of notification of risk of breast, ovarian, and colorectal cancer [9]. The components of the criteria for screening include knowledge of the disease, knowledge of test, treatment of disease, and cost of the test. While the workshop primarily considered testing for genetic susceptibility to cancer, the new criteria should be valuable in the consideration of other genetic susceptibility testing.

Thrombophilia screening meets some but not all of the proposed criteria. For example, the burden of VTE is significant but the risk in children is quite low. There are suitable tests for screening, but there may not be consensus on management for those with positive test results.

Thrombophilia screening

Thrombophilia screening is a matter of debate [10–13] and there are a variety of screening guidelines. The American College of Medical Genetics (ACMG) published consensus statements on factor V Leiden (FVL) and prothrombin G20210A (PT) gene mutation testing [14,15]. These statements do not recommend random screening of the general population or prenatal or routine newborn screening. According to the ACMG, genetic screening for risk for thrombosis should be offered for relatives of individuals with